

Ultraviolet B radiation mediated generation of Platelet-activating factor agonists augments melanoma tumor growth

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Platelet-activating factor (1-alkyl-2-acetyl-glycerophosphocholine; PAF) is a potent lipid mediator with diverse activities. Our previous studies have demonstrated that oxidized glycerophosphocholines (OxGPCs) that act as agonists for the Platelet-activating factor receptor (PAF-R) mediate ultraviolet B radiation (UVB) induced systemic immunosuppression in a process involving IL-10. However, the exact role of UVB-mediated systemic immunosuppression in pathophysiological processes remains unclear. The current studies sought to define whether UVB-induced systemic immunosuppression could modulate experimental murine melanoma tumor growth. Using a murine UVB model of systemic immunosuppression, we demonstrate that UVB exposure to a remote site from skin implanted with subcutaneous B16F10 melanoma results in enhanced tumor growth in C57BL/6 (wild-type) mice but not in PAF-R-deficient mice. We further show that intraperitoneal injection of the PAF agonist carbamoyl-PAF (CPAF) mimicked the UVB effect. Interestingly, neutralizing antibody against IL-10 blocked both CPAF- and UVB-mediated augmentation of B16F10 tumor growth. The next studies were designed to define whether the PAF-R effect was due to direct effects on B16F10 cells. Of note, B16F10 cells lack functional PAF-R expression. To address this question, we first generated PAF-R expressing B16F10 (B16-PAFR) and its vector control B16-MSCV cells by retroviral transduction and confirmed the presence of PAF-R in B16-PAF-R cells by intracellular Ca²⁺ flux in response to CPAF and qRT-PCR. Transplantation of B16-PAFR cells into mice did not result in an increased rate of tumor growth over control B16-MSCV cells either alone, or in response to UVB or CPAF. These studies provide a novel unreported effect of UVB-mediated PAF agonists, namely, that they can augment melanoma tumor growth via IL-10.